

REMARKS/ARGUMENTS

Claims 1-8, 12-16 and 22-23 are pending in the application. Claim 2 has been cancelled. Claims 1, 3, 4, and 22 have been amended. Support for the amendments can be found in the specification as well as in the original claims. No new matter has been added by way of amendment. Re-examination and reconsideration of the claims as amended are requested.

**The Rejection of Claims Under 35 U.S.C. §112, First Paragraph,
Should Be Withdrawn**

The Office Action (7/1/03, page 2, #4) has rejected claims 1-8, 12-16, and 22-23 under 35 U.S.C. §112, first paragraph, "as containing subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention." Applicants respectfully traverse this rejection.

The Office Action states (page 2) that the rejection is repeated for reasons of record. The Office Action also states that Applicants' citation of Bulet and Cho is unpersuasive and that Appendix A and B could not be evaluated because "[i]t is not clear in Appendix A what the sequences in the lower portion are" and in Appendix B, the "significance of the capital letters vs the lower case letters in the alignment" was not clear.

As the Office Action of 11/21/02 (paper #10) acknowledged, the *Vaejovis carolinianus* defensin (SEQ ID NO:4) shares 75.7% identity to a previously-identified defensin from the scorpion *Androctonus australis hector* (Office Action at p. 3). However, this Office Action stated that "SEQ ID NO:4 has **only** 75.7% identity to the defensin from *Androctonus australis hector*" (emphasis added) and concluded that "[t]he specification provides no evidence that SEQ ID NO:4 actually encodes a protein with defensin activity." (Office Action of 11/21/02 at p. 4).

In response, Applicants respectfully disagreed with this conclusion and noted that they had provided art-accepted methods to establish that the *Vaejovis carolinianus* polypeptide of SEQ ID NO:4 is a defensin. First, *V. carolinianus* SEQ ID NO:3 encodes the protein of SEQ ID NO:4, which shares 75.7% sequence identity with a defensin from *Androctonus australis hector* (see Example 3, pp. 23-25 of the specification). The polypeptide of SEQ ID NO:4 is cationic,

with a predicted pI of 9.44 (see Appendix C, analysis of SEQ ID NO:4 using ExPASy software). Further, the polypeptide of SEQ ID NO:4 contains the conserved cysteine residues found in insect defensins. These conserved cysteine residues are well-known in the art and, as indicated in Applicants' previous response, are discussed in the Bulet and Cho references. For example, Bulet *et al.* (1999) (*Dev. Comp. Immunol.* 23: 329-344) discusses:

[A] striking feature ... emerges from the comparison of the three-dimensional structures of insect defensins,...a motif named "Cysteine Stabilized α -helix (CSH). This scaffold refers to an invariant Cys-Xaa-Cys sequence found in a strand of a β -sheet in which two cysteine residues are attached to two cysteine residues of the stretch Cys-Xaa-Xaa-Xaa-Cys present in an α -helix...."

(Bulet *et al.* (1999), *ibid.*, pp. 334-335). Cho *et al.* (1995) (*Insect Biochem. Mol. Biol.* 26: 395-402) presents a diagram of these common motifs of cysteine residues in a multiple alignment of insect and scorpion defensins (p. 399, Figure 2). As stated in Applicants' previous response, Appendix A "reproduces Figure 1 of the present specification above a portion of Cho's Figure 2; dashed lines indicate conserved cysteines also highlighted by Cho; highlighted residues are conserved cysteines." As also noted previously, the exemplary disclosed sequence of SEQ ID NO:4 contains all six of these conserved cysteine residues.

Applicants believe that the explanation of Appendix A was clear and would be readily understood by one of skill in the art. Applicants note that the Cho reference has been provided along with Applicants' responses. However, for the convenience of the Examiner, Cho's legend for Figure 2 is as follows:

FIGURE 2. Amino acid sequence alignment of insect and scorpion defensins. Deduced amino acid sequences from *Aedes aegypti* (*Aed ae*, yello fever mosquito), *Phormia terranova* (*Pho te*, black blowfly), *Sarcophaga peregrina* (*Sar pe*, fleshfly), *Drosophila melanogaster* (*Dro me*, fruit fly), *Apis mellifera* (*Api me*, honey bee), *Tenebrio molitor* (*Ten mo*, darkling beetle), *Zophobas atratus* (*Zop at*, beetle), *Pyrrhocoris aptarus* (*Pyr ap*, red bug), *Aeschna cyanea* (*Aes cy*, dragonfly) and (*Leiurus quinquestriatus*, [*Lei qu*,] scorpion) were analyzed with the PileUp program. Mosquito defensin A variants are denoted as A1, A2, A3, and A4. *Aed ae* (B) and *Aed ae* (C) are mosquito defensin B and C isoforms taken from Lowenberger *et al.* (1995). Gap characters in sequences were inserted by PileUp to create the optimal alignment. Dots

before the sequence are due to the unavailability of their pre-propeptide sequences. Arrowheads indicate the signal peptide and propeptide cleavage sites based on the analysis of mosquito defensins. Nucleotide variations found in AaDef A cDNAs (Fig. 1B) resulted in several amino acid changes which are in bold letters. Amino acid substitutions referring to mosquito defensin isoforms are double underlined. Six cysteines engaged in disulfide bond formation are marked in reverse phase. Paired disulfide-linked cysteines are connected with thick lines. There are three predicted domains: an N-terminal loop (residues 1-13 counted from the N-terminus of the mature defensin, the hatched box), an α -helix (residues 14-24, the grid box) and an anti-parallel β -sheet (residues 27-40, open arrows).

Thus, Appendix A's comparison of the sequences in Figure 1 of the present application, including SEQ ID NO: 4, to the conserved cysteines diagrammed in Cho's Figure 2 makes clear that all of the described defensin motifs involving cysteines are contained within SEQ ID NO:4.

Appendix B further supports the identification of the polypeptide of SEQ ID NO:4 as a defensin. As discussed in Applicants' previous response, the polypeptide of SEQ ID NO:4 was compared to the Pfam database of protein families and showed a high degree of sequence similarity with the consensus structure for Arthropod defensins (PFAM Accession No. PF01097; see Appendix B). As described on the Pfam website and references cited thereon, alignments marked "!!" (like the alignment shown in Appendix B) are very significant hits above the Pfam gathering cutoffs. In addition, an expectation value or E-value below 0.05 indicates a significant hit; the E-value of the alignment of 4.8×10^{-12} is a very significant hit. The visual representation of the alignment essentially uses capital letters to represent residues that were aligned to the consensus sequence.

As described in the Pfam database (see page 2 of Appendix B), the Arthropod defensin family is "a family of insect and scorpion cysteine-rich antibacterial peptides, primarily active against Gram-positive bacteria (see Appendix B). The Pfam database provides a curated collection of well-characterized protein family domains with high quality alignments. Functional domains of novel proteins may be identified by comparison with the Pfam protein family domain alignments. It is well known in the art that regions of sequence homology with known functional domains may be used to determine protein function. Accordingly, the presence of a Pfam

consensus structure for the Arthropod defensin family in the *V. carolinianus* sequence of SEQ ID NO:4 indicates that this polypeptide functions as a defensin.

Applicants again note that the United States Patent and Trademark Office accepts sequence homology as a basis for establishing utility. While here the rejection is characterized as being an enablement rejection under 35 U.S.C. §112, first paragraph, such rejections are typically made under both 35 U.S.C. §101 and 35 U.S.C. §112. The rationale for such rejections is that a sequence has no utility if it has no known function and therefore one of skill in the art would not know how to use it. Here, the rejection was made only under 35 U.S.C. §112, first paragraph, but the rejection hinges on whether the specification provides evidence that SEQ ID NO:4 actually encodes a protein with defensin activity. The present Office Action (page 3, paragraph 4) states that “[t]his is a rejection made under 35 USC 112, so Applicant’s arguments regarding the Utility Training Guidelines are moot.” Applicants are unclear as to why this rejection is made under the label of enablement. In the present case, the Examiner has not accepted the asserted utility for the claimed invention but has failed to provide sufficient evidence or sound scientific reasoning to rebut Applicants’ assertions. However, whether this rejection is labeled as a rejection for lack of utility, written description, or enablement, Applicants believe that one of skill in the art would accept the evidence provided as proof that the polypeptide of SEQ ID NO:4 was a defensin.

The Office Action (page 4) asserts that Applicants’ arguments that one of skill in the art would accept that SEQ ID NO:4 functions as a defensin are not persuasive because the Broekaert, Terras, and Thevissen references “are directed toward a radish anti-fungal peptide and present no comparisons to Arthropod defensin” and because “[t]he peptide isolated by Lamberty et al unexpectedly lacks antibacterial activity (pg 9325, right column, paragraph 3).”

Applicants are confused by these statements and by the assertion that these statements support the conclusion that the proteins of the claims are not defensins. While the peptide isolated by Lamberty *et al.* apparently lacks antibacterial activity, this does not mean that it is not a defensin. Defensins are known to vary in their antimicrobial activity. As discussed later in the same paragraph of the Lamberty reference cited by the Office Action (page 9325, col. 2, second paragraph), “heliomicin is active against most of the filamentous fungi tested....” The Lamberty

reference concludes, “the antifungal activity observed for the *Heliothis* peptide prompts us to classify heliomycin in the group of antifungal peptides such as plant defensins....” As noted in the Hetru reference, “[i]nsect defensins are mainly active against Gram-positive bacteria, but some activity is occasionally recorded against Gram-negative bacteria or fungi.” (page 45, second paragraph under the heading “Insect Defensins.”) As noted in the Thevissen reference, “[s]everal members of the plant defensin family inhibit the growth of a broad range of fungi at micromolar concentrations....” (page 15018, col. 2, first full paragraph) Thus, it is known in the art that defensins have a range of antimicrobial activities; it is not required that a molecule have antibacterial activity to be considered a defensin.

The Lamberty, Terras, and Thevissen are examples of references that provide particular support for the well-established principle that sequence homology is a predictor of protein function. Defensins are described in the art as genes which contain the characteristic conserved cysteines, and defensin gene families are described as sharing properties of relatively short length and amino acid similarities from 58% to 95%. See, e.g., Bulet *et al.* (1999) *Dev. Comp. Immunol.* 23: 329-344 at pp. 330-331; Cho *et al.* (1995) *Insect Biochem. Mol. Biol.* 26: 395-402; White *et al.* (1995) *Curr. Op. Struct. Biol.* 5: 521-527; Broekaert *et al.* (1995) *Plant Physiol.* 108: 1353-1358. Furthermore, functional assays that have been performed on proteins having these properties have confirmed that such proteins have defensin activity. See, e.g., Lamberty *et al.* (1999) *J. Biol. Chem.* 274: 9320-9326; Thevissen *et al.* (1999) *App. Env. Microbiol.* 65: 5451-5458; Terras *et al.* (1995) *Plant Cell* 7: 573-588. Terras *et al.* characterized defensins from radish seed, Thevissen *et al.* characterized the response of *N. crassa* hyphae to anti-fungal plant defensins from *Aesculus hippocastanum*, *Dahlia merckii* and *Heuchera sanguinea*, and Lamberty *et al.* characterized a defensin isolated from the lepidopteran *Heliothis virescens*.

All three of these references teach assays for defensins and illustrate that peptides having defensin sequence similarity have been found to have defensin activity. These examples, which demonstrate the accuracy of sequence similarity-based determinations of protein function, represent only a few of the many such instances that are found in the scientific literature. Because of evidence such as that presented above, methods of using sequence homology within the functional domains of proteins of known function to determine the function of novel proteins

have become widely accepted by those of skill in the art as reliable and accurate. Accordingly, one of skill in the art would readily accept that the *V. carolinianus* protein of SEQ ID NO:4 functions as a defensin based on the types of evidence presented in the specification.

The Office Action (page 5, first paragraph) again asserts that the Pang and Barton references point to unpredictability. Applicants again respectfully disagree and note that the functional limitation of the present claims is that the polypeptide has defensin activity, not insecticidal activity. Defensins need not be expressed in plants to exhibit their antimicrobial activity. For example, defensins show antibacterial and antifungal activity in liquid growth cultures of bacteria and fungi (see, for example, Lamberty *et al.* and Thevissen *et al.*, *op. cit.*). The Pang and Barton references both attempted to express insect-specific toxins—not defensins—in plants to engineer insect resistance. The present claims are not directed to engineering insect resistance in plants. Applicants note that, for example, claims 1-6 are drawn to isolated polynucleotides. Therefore, the Pang and Barton references are not relevant to the present claims.

Applicants further note that the Office Action states that

The protein described by Terras et al was not transgenically expressed in a plant—the antifungal assays were done with endogenously expressed protein—and thus has no relevance to the portion of the enablement rejection directed to unpredictability of expression of these proteins in plants.

This statement is incorrect. The Terras reference teaches that radish defensins, when expressed in transgenic tobacco, conferred enhanced resistance to the foliar fungal pathogen *Alternaria longipes*. These experiments are discussed in detail beginning on page 578 (col. 2). Experiments *in planta* are described beginning on page 579 (col. 2). Thus, defensins when expressed in plants have been shown to display defensin activity and to confer enhanced disease resistance.

The Office Action states that Applicants have not pointed to guidance in the specification for which regions of SEQ ID NO:4 can be altered. However, Applicants have provided such guidance, as demonstrated by Appendix A and B of the previously-filed response. Appendix A shows the location of conserved cysteine residues, and Appendix B shows the location of the

arthropod defensin consensus sequence in SEQ ID NO:4. In addition, Applicants have provided exemplary full-length nucleotide and amino acid sequences of defensins from *Scolopendra canidens* (SEQ ID NOs: 1 and 2, respectively), *Vaejovis carolinianus* (SEQ ID NOs: 3 and 4), and *Argiope* spp. (nucleotide sequences set forth in SEQ ID NOs: 5, 7, and 9; amino acid sequences set forth in SEQ ID NOs: 6, 8, and 10, respectively). SEQ ID NO:3 from *V. carolinianus* encodes a protein (SEQ ID NO:4) with 75.7% identity to a defensin from *Androctonus australis hector* (see Table 4, page 24).

The Office Action concludes that an undue amount of experimentation would be required to make a nucleotide sequence that encodes a polypeptide which is at least 90% identical to SEQ ID NO:4. Applicants note that independent claim 1 (and hence claims 3-8, 12-16, and 22, which are dependent on or incorporate the limitations of claim 1) has been amended to recite that the nucleotide sequence encodes a polypeptide that has an amino acid sequence that is at least 95% identical to the amino acid sequence set forth in SEQ ID NO:4. Independent claim 1 also requires that the polypeptide have defensin activity. Independent claim 23 recites that the polynucleotide specifically hybridizes to the complement of the sequence of SEQ ID NO:3 under particular conditions and that the polypeptide has defensin activity.

Applicants believe that those of skill in the art, provided the guidance in the present specification, could readily make and use the claimed invention. Guidance for determining percent identity of sequences is provided in the specification, for example, on pages 8-9. Those of skill in the art can readily determine the nucleic acid sequence of a nucleic acid molecule as well as the percent identity between sequences.

Moreover, claim 1 specifies that the polypeptide of the method has defensin activity and therefore encompasses functional variants. As discussed in detail above, defensins are well-known in the art and are known to provide protection to transgenic plants (see specification, *e.g.*, on pp. 1, 2 and 16). Assays and procedures are known in the art to readily determine whether a sequence has defensin activity (see specification pp. 16-17). For example, Terras *et al.* (1995) (*Plant Cell* 7:573-588) teaches an assay for defensin antifungal activity from germinating plant seeds (p. 574, col. 1 and Figure 1) as well as tissue-print immunolocalization assays for monitoring expression of defensins in various plant parts (p. 575, col. 2), assays for the enhanced

disease tolerance of transgenic plants expressing defensins (p. 578, col. 2-p.580), and assays of *in vitro* defensin activity from transgenic plants (p. 580, col. 2). Other references teach assays for expression of particular genes; for example, Oh *et al.* (1999) *Plant Mol. Biol.* 41:313-319 teaches assays for determining whether the expression of particular genes has been induced by various treatments. Thevissen *et al.* (1996) *J. Biol. Chem.* 271: 15018-15025 teaches assays for antifungal activities of defensins, and Thevissen *et al.* (1999) *App. Env. Microbiol.* 65: 5451-5458 teaches an assay for permeabilization of fungal membranes by defensins. Lamberty *et al.* (1999) *J. Biol. Chem.* 274: 9320-9326 teaches assays for antifungal and antibacterial activities of defensins.

Thus, guidance is provided as to which region of the sequence of SEQ ID NO:4 can be altered and still provide a polypeptide species encompassed by the claim. Applicants have provided the exemplary nucleotide sequence of SEQ ID NO:3 and the exemplary amino acid sequence of SEQ ID NO:4. The claimed sequences of the invention vary from this sequence by structural parameters (*i.e.*, percent sequence identity to SEQ ID NO:4, or encoding such a polypeptide) and are required to retain defensin activity.

Thus, a rational scheme for determining the regions of the defensin polypeptides encoded by the claimed sequence that would tolerate modification is provided. Based on the exemplary defensin nucleotide and polypeptide sequences provided and the known methods for identifying additional residues critical for defensin activity, the skilled artisan could choose among possible modifications to produce polypeptides within the parameters set forth in the claims and then test these modified variants to determine if they retain defensin activity.

As discussed in detail in their previous response, Applicants believe that undue experimentation would not be required for one of skill in the art to make and use the claimed invention. The standards for assessing whether undue experimentation is necessary have been discussed in *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988) and *In re Jackson*, 217 USPQ 804, 807 (Bd. Pat. App. & Int. 1982), and Applicants believe that those standards when properly applied to the present situation lead to the conclusion that undue experimentation would not be required here.

Here, the practice of the invention requires essentially two steps: generating a polynucleotide having a sequence that meets the applicable limitations of the claims and assaying the encoded polypeptide for defensin activity. Guidance for performing these steps is provided in the specification and well-known in the art. The additional embodiments of the dependent claims incorporate further limitations which are also taught in the specification and readily created by those of skill in the art. Ample guidance is therefore provided to allow one of skill in the art to identify additional sequences encompassed by the claims. Consequently, the quantity of experimentation necessary and the amount of guidance presented in the specification is sufficient to enable the claimed polynucleotides and their methods of use as set forth in the claims. Therefore, Applicants respectfully request that the rejection of the claims under 35 U.S.C. §112, first paragraph, be withdrawn.

The Office Action (11/21/02, page 6, #9) has rejected claims 1-8, 12-16, and 22-23 under 35 U.S.C. §112, first paragraph, "as containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention." The Office Action states that this rejection is repeated for the reasons of record. Applicants again respectfully traverse this rejection.

Independent claim 1 (and thereby claims 1-8, 12-16, and 22, which are dependent on or incorporate the limitations of claim 1) has been amended to recite that the nucleotide sequence encodes a polypeptide that has an amino acid sequence that is at least 95% identical to the amino acid sequence set forth in SEQ ID NO:4. Applicants also note that independent claim 1 requires that the polypeptide have defensin activity. Support for these amendments can be found in the original claims and in the specification, more particularly, for example, on pages 2, 14, and 18. Independent claim 23 recites that the polynucleotide specifically hybridizes to the complement of the sequence of SEQ ID NO:3 under particular conditions and that the polypeptide has defensin activity.

Amended independent claim 1 recites that the polypeptide encoded by the claimed polynucleotide has at least 95% identity to the sequence set forth in SEQ ID NO:4. The

recitation of at least 95% sequence identity is a *very predictable structure* of the sequences encompassed by the claimed invention. Applicants note that the description of a representative number of species does not require the description to be of such specificity that it would provide individual support for each species that the genus embraces. 66 Fed. Reg. 1099, 1106 (2001). Satisfactory disclosure of a "representative number" depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed. 66 Fed. Reg. 1099, 1106 (2001). Applicants submit that the knowledge and level of skill in the art would allow a person of ordinary skill to envision the claimed invention, *i.e.*, a nucleotide sequence encoding a polypeptide having at least 95% sequence identity to the sequence set forth in SEQ ID NO:4.

Furthermore, the description of a claimed genus can be by structure, formula, chemical name, or physical properties. *See, Ex parte Maizel*, 27 USPQ2d 1662, 1669 (B.P.A.I. 1992), citing *Amgen v. Chugai*, 927 F.2d 1200, 1206 (Fed. Cir. 1991). A genus of DNAs may therefore be described by means of a recitation of a representative number of DNAs defined by nucleotide sequence and falling within the scope of the genus, *or* by means of a recitation of structural features common to the genus, which features constitute a substantial portion of the genus. *See, Regents of the University of California v. Eli Lilly & Co.*, 119 F.3d 1559, 1569 (Fed. Cir. 1997); *see also* Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, First Paragraph, "Written Description" Requirement, 66 Fed. Reg. 1099, 1106 (2001) (referred to hereafter as "Guidelines.") The recitation of a predictable polypeptide structure of at least 95% sequence identity to SEQ ID NO:4 is sufficient to satisfy the written description requirement.

The Office Action (page 8) states that "Applicant urges that *Eli Lilly* and *Amgen* do not apply to the present situation...." Applicants disagree with this conclusion. Rather, Applicants believe that the claims meet the written description requirement as clarified by *Eli Lilly* and *Amgen*. Applicants have provided exemplary sequences of the invention as set forth in SEQ ID NOs:3 and 4. Applicants have thus provided a structural definition of the sequences of the invention. In addition, because defensins are well-known in the art, those of skill in the art can readily assess whether a nucleic acid molecule meeting the sequence element of the claims also

meets the functional limitation element of the claims. This is what *Eli Lilly* requires. Thus, Applicants have also conceived the sequences of the invention as articulated in *Amgen*; that is, Applicants are able “to envision the detailed constitution of a gene so as to distinguish it from other materials, as well as a method for obtaining it.” *Amgen*, 18 USPQ2d at 1021.

In addition to structural characteristics, an Applicant may also rely upon functional characteristics in the description, provided there is a correlation between the function and structure of the claimed invention. See “Guidelines,” citing *Lilly* at 1568. Indeed, independent claim 1 recites functional characteristics of the claimed genus. Specifically, claim 1 recites that the claimed sequences further encode a polypeptide that has defensin activity; thereby providing a functional characterization of the sequences claimed in the genus. As discussed in more detail above and as indicated in the specification (see, *e.g.*, pp. 16-17), those of skill in the art are familiar with assays to determine whether a particular polypeptide has defensin activity.

Example 14 of the “Synopsis of Application of Written Description Guidelines” is directed to a generic claim: a protein having at least 95% sequence identity to the sequence of SEQ ID NO:3, wherein the sequence catalyzes the reaction $A \rightarrow B$. The synopsis materials conclude that the generic claim of Example 14 is sufficiently described under § 112, first paragraph, because: 1) “the single sequence disclosed in SEQ ID NO:3 is representative of the genus”; and 2) the claim recites a limitation requiring the compound to catalyze the reaction from $A \rightarrow B$. The synopsis materials conclude that one of skill in art would recognize that the Applicants were in possession of the necessary common attributes possessed by the members of the genus.

Following the analysis of Example 14, Applicants submit that the present claims satisfy the written description requirements of § 112, first paragraph. Specifically, the claims of the present invention encompass a polynucleotide having a sequence encoding a polypeptide having at least 95% sequence identity to SEQ ID NO:4. As in Example 14, the specification discloses the nucleic acid sequence of SEQ ID NO:3 and the amino acid sequence of SEQ ID NO:4 and independent claim 1 recites a limitation requiring the compound to have a specific function (*i.e.*, defensin activity). Consequently, contrary to the conclusion in the Office Action, the sequences encompassed by genus claim 1 are defined by relevant identifying physical and chemical properties.

In fact, the common attributes or features of the elements possessed by the members of the genus is that they encode polypeptides having defensin activity and sharing at least 95% sequence identity to the amino acid sequence of SEQ ID NO:4. Thus, the necessary common features of the claimed genus are clear. Similarly, the sequences encompassed by claim 23 are defined by relevant properties; *i.e.*, by hybridization under specified conditions and by encoding a polypeptide having defensin activity.

In summary, the description of a representative number of species *does not* require the description to be of such specificity that it would provide individual support for each species that the genus embraces. Applicants submit that the relevant identifying physical and chemical properties of the disclosed genus would be clearly recognized by one of skill in the art and consequently, the Applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus. Accordingly, the rejection of claims 1-8, 12-16, and 22-23 under 35 U.S.C. §112, first paragraph, for lack of written description should be withdrawn and not applied to the newly submitted claims.

The Rejection of Claims Under 35 U.S.C. §112, Second Paragraph,

Should Be Withdrawn

The Office Action (page 8, #6) has rejected claim 22 as being indefinite due to a defect in antecedent basis. The claim has been amended to address these rejections, and Applicants respectfully submit that this rejection has been obviated by amendment.

CONCLUSION

In view of the above amendments and remarks, Applicants submit that the rejections of the claims under 35 U.S.C. §§112, first and second paragraphs, are overcome. Applicants respectfully submit that this application is now in condition for allowance. Early notice to this effect is solicited.

If in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject Application, the Examiner is invited to call the undersigned.

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Filed: 4/10/2001

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It is not believed that extensions of time or fees for net addition of claims are required, beyond those that may otherwise be provided for in documents accompanying this paper. However, in the event that additional extensions of time are necessary to allow consideration of this paper, such extensions are hereby petitioned under 37 CFR § 1.136(a), and any fee required therefore (including fees for net addition of claims) is hereby authorized to be charged to Deposit Account No. 16-0605.

Respectfully submitted,

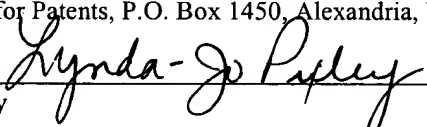


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Date of Deposit August 28, 2003

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RTA 2140872v1